We claim:

1. A method of promoting angiogenesis in a subject animal comprising administering to the subject an angiogenic amount of a hedgehog polypeptide or agonist thereof.

2. The method of claim 1, wherein the step of administering comprises contacting the hedgehog polypeptide or agonist with a mesenchymal cell of the subject.

3. The method of claim 1, comprising administering to the subject a polypeptide including a hedgehog amino acid sequence, which hedgehog sequence directs the binding of the polypeptide to a patched receptor polypeptide and/or induces alkaline phosphatase activity in C3H10T1/2 cells.

4. The method of claim 1, comprising administering to the subject a polypeptide including a hedgehog amino acid sequence having at least 60% amino acid identity with SEQ ID No. 10-18 or 20.

5. The method of claim 1, comprising administering to the subject a polypeptide including a hedgehog amino acid sequence encoded by a coding sequence which hybridizes under stringent conditions to any of SEQ ID No. 1-9 or 19.

6. The method of claim 1, comprising administering to the subject a polypeptide including a hedgehog amino acid sequence represented by SEQ ID No. 26.

7. The method of any of claims 3 – 7, wherein the hedgehog sequence includes at least 50 resdiues of an extracellular domain of a hedgehog protein.

8. The method of any of claims 3 – 7, wherein the polypeptide is derivatized with one or more chemical moieties.

9. The method of claim 8, wherein the chemical moiety is a polyalkylene glycol polymer.

10. The method of claim 8, wherein the chemical moiety is a hydrophobic moiety.

11. The method of claim 10, wherein the hydrophobic moiety is a lipid.

12. The method of claim 8, wherein the chemical moiety is one or more phosphate groups.

13. The method of claim 8, wherein the chemical moiety is one or more acetyl groups.

14. The method of claim 8, wherein the chemical moiety is one or more sugar or carbohydrate groups.

15. The method of claim 8, wherein the chemical moieties are any combination of phosphate, acetyl, sugar, carbohydrate, or hydrophobic moieties.

16. The method of claim 4, wherein the method further comprises administering an agent that enhances agonistic properties of the hedgehog therapeutic.

17. The method of claim 16, wherein the agent is an angiogenic factor selected from the group consisting of vascular endothelial growth factor (VEGF), hepatocyte growth factor (HGF), basic fibroblast growth factor (bFGF), angiopoietin 1, angiopoietin 2, monocyte chemotactic protein-1 (MCP-1).

18. A method of inhibiting angiogenesis in a subject animal comprising administering to the subject an antiangiogenic amount of a hedgehog antagonist.

19. The method of claim 18, comprising administering a polypeptide including one or more antigen binding domains which bind to and inhibit hedgehog signalling.

20. The method of claim 18, comprising administering a polypeptide including one or more antigen binding domains which bind to <u>patched</u> and inhibit hedgehog signalling.

21. The method of claim 18, comprising administering a polypeptide including one or more antigen binding domains which bind to <u>smoothened</u> and inhibit hedgehog signalling.

22. The method of claim 19, 20 or 21, wherein the antigen binding domain is part of a an antibody structure selected from the group consisting of a humanized antibody homology, a human antibody homolog, a chimeric antibody homolog and fragments thereof.

23. The method of claim 18, comprising administering a functional antagonist of a hedgehog therapeutic.

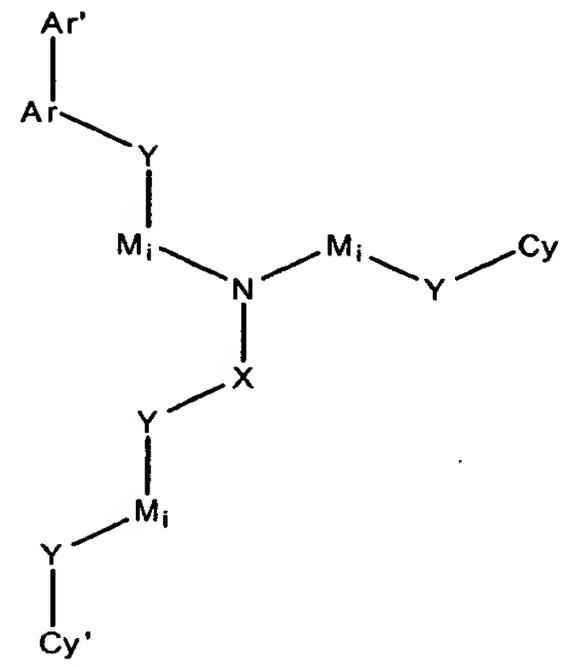
24. The method of claim 18, or 20, wherein the subject has a condition selected from the group consisting of a malignant tumor, retinopathy, macular degeneration, a nonmalignant tumor, rheumatoid arthritis, osteoarthritis, neovascular glaucoma, keloids, Crohn's disease, ulcerative colitis, and psoriasis.

25. The method of claim 1, wherein the hedgehog agonist is a small organic molecule.

26. The method of claim 25, wherein the hedgehog agonist has a molecular weight less than 2500 amu.

27. The method of claim 25, wherein the hedgehog agonist is represented by general formula (XII):

Formula XII



wherein, as valence and stability permit,

Ar and Ar' independently represent substituted or unsubstituted aryl or heteroaryl rings;

Y, independently for each occurrence, may be absent or represent -N(R)-, -O-, -S-, or -Se-;

X can be selected from -C(=O)-, -C(=S)-, -S(O_2)-, -S(O)-, -C(=NCN)-, -P(=O)(OR_2)-, and a methylene group optionally substituted with 1-2 groups such as lower alkyl, alkenyl, or alkynyl groups;

M represents, independently for each occurrence, a substituted or unsubstituted methylene group, such as -CH_2-, -CHF-, -CHOH-, -CH(Me)-, -C(=O)-, etc., or two M taken together represent substituted or unsubstituted ethene or ethyne;

R represents, independently for each occurrence, H or substituted or unsubstituted aryl, heterocyclyl, heteroaryl, aralkyl, heteroaralkyl, alkynyl, alkenyl, or alkyl, or two R taken together may form a 4- to 8-membered ring, e.g., with N;

Cy and Cy' independenly represent substituted or unsubstituted aryl, heterocyclyl, heteroaryl, or cycloalkyl, including polycyclic groups;

i represents, independently for each occurrence, an integer from 0 to 5, preferably from 0 to 2; and

n, individually for each occurence, represents an integer from 0 to 10, preferably from 0 to 5.

28. The method of any of claims 3 – 7, comprising administering a nucleic acid sequence encoding the polypeptide.

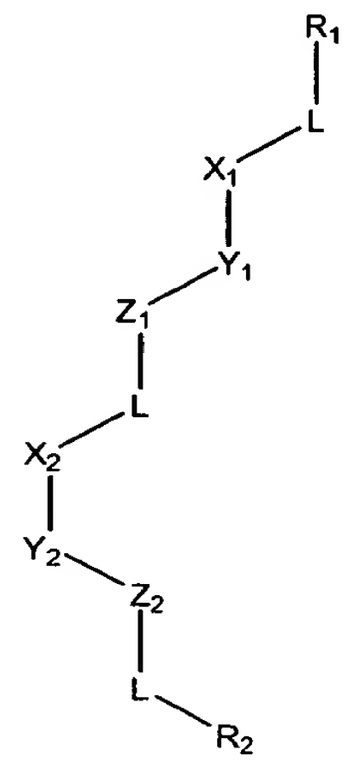
29. The method of claim 29, wherein the nucleic acid sequences encoding the polypeptide are introduced via a viral vector, via lipofection, and/or as naked DNA.

30. The method of claim 18, wherein the hedgehog antagonist is a small organic molecule.

31. The method of claim 30, wherein the hedgehog antagonist has a molecular weight less than 2500 amu.

32. The method of claim 30, wherein the hedgehog antagonist is represented by one or more of formulas I – XI.

33. The method of claim 30, wherein the hedgehog antagonist is represented by general formula (I):



wherein, as valence and stability permit,

R_1 and R_2, independently for each occurrence, represent H, lower alkyl, aryl (e.g., substituted or unsubstituted), aralkyl (e.g., substituted or unsubstituted, e.g., -$(CH_2)_n$aryl), or heteroaryl (e.g., substituted or unsubstituted), or heteroaralkyl (e.g., substituted or unsubstituted, e.g., -$(CH_2)_n$heteroaralkyl-);

L, independently for each occurrence, is absent or represents -$(CH_2)_n$-alkyl, -alkenyl-, -alkynyl-, -$(CH_2)_n$alkenyl-, -$(CH_2)_n$alkynyl-, -$(CH_2)_nO(CH_2)_p$-, -$(CH_2)_nNR_2(CH_2)_p$-, -$(CH_2)_nS(CH_2)_p$-, -$(CH_2)_n$alkenyl$(CH_2)_p$-, -$(CH_2)_n$alkynyl$(CH_2)_p$-, -$O(CH_2)_n$-, -$NR_2(CH_2)_n$-, or -$S(CH_2)_n$-;

X_1 and X_2 can be selected, independently, from -$N(R_8)$-, -O-, -S-, -Se-, -N=N-, -ON=CH-, -(R_8)N-$N(R_8)$-, -$ON(R_8)$-, a heterocycle, or a direct bond between L and Y_1 or Y_2, respectively;

Y_1 and Y_2 can be selected, independently, from -C(=O)-, -C(=S)-, -$S(O_2)$-, -S(O)-, -C(=NCN)-, -P(=O)(OR_2)-, a heteroaromatic group, or a direct bond between X_1 and Z_1 or X_2 and Z_2, respectively;

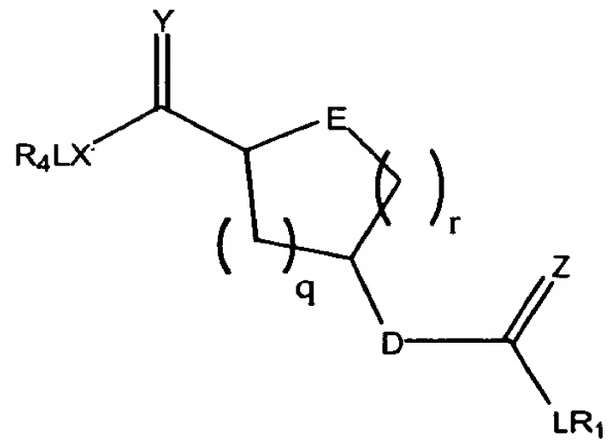
Z_1 and Z_2 can be selected, independently, from -$N(R_8)$-, -O-, -S-, -Se-, -N=N-, -ON=CH-, -R_8N-NR_8-, -ONR_8-, a heterocycle, or a direct bond between Y_1 or Y_2, respectively, and L;

R_8, independently for each occurrence, represents H, lower alkyl, -$(CH_2)_n$aryl (e.g., substituted or unsubstituted), -$(CH_2)_n$heteroaryl (e.g., substituted or unsubstituted), or two R_8 taken together may form a 4- to 8-membered ring, e.g., with X_1 and Z_1 or X_2 and Z_1, which ring may include one or more carbonyls;

p represents, independently for each occurrence, an integer from 0 to 10, preferably from 0 to 3; and

n, individually for each occurence, represents an integer from 0 to 10, preferably from 0 to 5.

34. The method of claim 30, wherein the hedgehog antagonist is represented by general formula (VI):



Formula VI

wherein, as valence and stability permit,

R_1, R_2, R_3, and R_4, independently for each occurrence, represent H, lower alkyl, -$(CH_2)_n$aryl (e.g., substituted or unsubstituted), or -$(CH_2)_n$heteroaryl (e.g., substituted or unsubstituted);

L, independently for each occurrence, is absent or represents -$(CH_2)_n$-, -alkenyl-, -alkynyl-, -$(CH_2)_n$alkenyl-, -$(CH_2)_n$alkynyl-, -$(CH_2)_nO(CH_2)_p$-, -$(CH_2)_nNR_8(CH_2)_p$-, -$(CH_2)_nS(CH_2)_p$-, -$(CH_2)_n$alkenyl$(CH_2)_p$-, -$(CH_2)_n$alkynyl$(CH_2)_p$-, -$O(CH_2)_n$-, -$NR_8(CH_2)_n$-, or -$S(CH_2)_n$-;

X and D, independently, can be selected from -$N(R_8)$-, -O-, -S-, -$(R_8)N$-$N(R_8)$-, -$ON(R_8)$-, or a direct bond;

Y and Z, independently, can be selected from O or S;

E represents O, S, or NR_5, wherein R_5 represents LR_8 or -(C=O)LR_8.

R_8, independently for each occurrence, represents H, lower alkyl, -$(CH_2)_n$aryl (e.g., substituted or unsubstituted), -$(CH_2)_n$heteroaryl (e.g., substituted or unsubstituted), or two R_8 taken together may form a 4- to 8-membered ring;

p represents, independently for each occurrence, an integer from 0 to 10, preferably from 0 to 3;

n, individually for each occurrence, represents an integer from 0 to 10, preferably from 0 to 5; and

q and r represent, independently for each occurrence, an integer from 0-2.